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TOWNSEND AND TOWNSEND AND CREW, LLP
TWO EMBARCADERO CENTER
EIGHTH FLOOR
SAN FRANCISCO, CA 94111-3834

EXAMINER
HILL, KEVIN KAI

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1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,657	DING ET AL.	
	Examiner	Art Unit	
	KEVIN K. HILL	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,40,41,43-53 and 75-78* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *38,40,41,43-53 and 75-78* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

Election/Restrictions

Applicant has elected without traverse the invention of Group I, Claims 38-53, drawn to a vitellogenin expression vector and a transgenic eukaryotic host cell comprising said expression vector.

Amendments

In the reply filed February 15, 2008, Applicant has cancelled Claims 1-37, 39, 42 and 54-74, amended Claims 38, 40, 43-45, and added new claims, Claims 75-78.

Claims 38, 40-41, 43-53 and 75-78 are under consideration.

Priority

This application is a 371 of PCT/SG03/00266, filed November 1, 2003 which claims benefit of the parent provisional application 60/425,263, filed November 12, 2002. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged.

Claim Objections

1. **The prior objection to Claims 38 and 44 are withdrawn** in light of Applicant's amendments to the claims to improve clarity and precision of the claims.

Claim Rejections - 35 USC § 101

2. **The prior rejection of Claim 44 under 35 U.S.C. 101 is withdrawn** in light of Applicant's amendment to the claim limiting its scope to transgenic yeast.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. **The prior rejection of Claims 38-44 and 48-53 under 35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement **is withdrawn** in light of Applicant's amendments to the claims limiting the nucleic acid to a vitellogenin cDNA comprising SEQ ID NO:1.

4. **Claims 45-47 stand and Claims 75-78 are newly rejected under 35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is maintained for reasons of record in the office action mailed September 17, 2007 and re-stated below. The rejection has been re-worded slightly based upon Applicant's amendment filed February 15, 2008.

The claimed invention is directed to an expression vector comprising a vitellogenin gene operably linked to a promoter. At issue for the purpose of written description requirements is the lack of written support in the specification for the genus of vitellogenin genes.

> *Vas-cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that Applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not clearly allow persons of ordinary skill in the art to recognize that (he or she) invented what is claimed." (See *Vas-cath* at page 1116).

The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see *In re Shokal* 113USPQ283(CCPA1957); *Purdue Pharma L.P. vs Faulding Inc.* 56 USPQ2nd 1481 (CAFC 2000).

In analyzing whether the written description requirement is met for genus claims, it is first determined whether a representative number of species have been described by their complete structure. In the instant case, SEQ ID NOs: 1-20 are the only nucleic acid species encoding vitellogenin whose complete structure is disclosed.

Next, then, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics (i.e. other than nucleotide sequence), specific features and functional attributes that would distinguish different members of the claimed genus. In the instant case, the only other identifying characteristic is that the vitellogenin gene would encode a polypeptide functionally equivalent to a reference vitellogenin polypeptide, wherein one or more amino acid deletions, substitutions, modifications or additions may be present. While the specification discloses that the genus of vitellogenin structural variants should retain normal biological function, the specification does not disclose the normal biological function for each of the vitellogenins identified in the art at the time of the invention (pg 7, [0032]). The art recognizes that the vitellogenin gene family comprises vitellogenin, DSC-4 (defecation suppressor of *clk-1*), APOB, (apolipoprotein B), apolipophorin I, apolipophorin II, and MTP/Mttp (microsomal triglyceride transfer protein), wherein family members share a common amino-terminal "vitellogenin domain" (Brandt et al, BioEssays 27:339-346, 2005; pg 343, Box 2). However, the known vitellogenins are not functionally equivalent and the breadth of their respective "biological functions" are not fully known. The specification does not teach

any modification to a nucleic acid encoding a vitellogenin polypeptide so as to provide the necessary guidance to the artisan as to what changes may be made in the polypeptide while retaining normal biological function to the vitellogenin genus.

The Revised Interim Guidelines state:

"The claimed invention as a whole may not be adequately described if the claims require an essential or critical element which is not adequately described in the specification and which is not conventional in the art" (col. 3, page 71434), "when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus", "in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (col. 2, page 71436).

An Applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

Possession may also be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the Applicant was in possession of the claimed invention. See, e.g., *Pfaff v. Wells Elecs., Inc.*, 525 U.S. 55, 68, 1 19 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998), *Regents of the University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997)*, *Amgen, Inc. v. Chugai Pharmaceutical*, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991) (one must define a compound by "whatever characteristics sufficiently distinguish it").

Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. See *Fiers v. Revel*, 25 USPQ2d 1602 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. *In Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Without a correlation between structure and function, the claim does little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *See Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406 ("definition by function … does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is").

The Applicant has not provided any description or reduction to practice of nucleic acids encoding a vitellogenin polypeptide besides SEQ ID NOs: 1-20. Based on the Applicant's specification, the skilled artisan cannot envision the detailed chemical structure of the nucleotide sequences of vitellogenin genes as defined by the specification and encompassed by the claims. The few species of nucleic acids specifically disclosed are not representative of the genus because the genus is highly variant.

Accordingly, this limited information is not deemed sufficient to reasonably convey to one skilled in the art that the Applicant is in possession of the broad genus of vitellogenin genes, besides those nucleic acids SEQ ID NOs:1-20 encoding vitellogenin polypeptides, at the time the application was filed.

Thus, for the reasons outlined above, it is concluded that the claims do not meet the requirements for written description under 35 U.S.C. 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Applicant's Arguments

Applicant argues that:

a) vitellogenins are very high-density proteins produced by **egg-laying** [emphasis added] animals as a yolk precursor protein. Thus, the normal biological function of 'vitellogenin', as a phospholipoglycoprotein precursor to egg yolk in egg-laying animals, is implicit in its art-accepted name, and this function would be so recognized by the skilled artisan. The mere fact that [a plurality of] mammalian proteins share some limited degree of homology with vitellogenins, such as those found in fish or birds, does not make them vitellogenins.

b) a search of the GenBank protein sequence database at the NCBI website using the term "vitellogenin" results in 771 protein sequences.

Applicant's argument(s) has been fully considered, but is not persuasive.

With respect to a), it appears that Applicant has confused the **pattern of gene expression** with the **structural and functional properties** of the polypeptide encoded by the gene. The pattern of gene expression is controlled by *cis*-acting enhancers and promoters outside of the nucleic acid sequences encoding the vitellogenin protein. Those of ordinary skill in the art recognize that evolution re-uses "old genes", expressing a given gene in different cells and tissues, at different times of development. Just because humans do not lay eggs does not mean

that humans do not encode a vitellogenin gene; rather, the art recognizes that the human genome encodes vitellogenin homologues (see (b) below).

If one were to heterologously or ectopically express the art-recognized human vitellogenin homologues in a transgenic egg-laying animal, e.g. the eggs of *Xenopus*, would they not possess the same structural and functional properties as the homologous *Xenopus* vitellogenin? Similarly, if one were to heterologously or ectopically express a human vitellogenin homologue via the instant expression vectors in yeast, would it not possess the same structural and functional properties as its homologous counterpart cloned from *Xenopus* when also heterologously or ectopically expressed in yeast? Clearly, yeast is not an egg-laying animal. Thus, what characteristics would structurally and functionally distinguish a Xenopus vitellogenin from its human vitellogenin in such an artificial expression system?

With respect to b), the Examiner acknowledges the plurality of 'hits' using Applicant's search term. The Examiner further notes that 29 of those 'hits' within Applicant's larger set are human homologues. As discussed above, the known vitellogenins are not functionally equivalent and the breadth of their respective "biological functions" are not fully known. The specification does not teach any modification to a nucleic acid encoding a vitellogenin polypeptide so as to provide the necessary guidance to the artisan as to what changes may be made in the polypeptide while retaining normal biological function to the vitellogenin genus.

5. **The prior rejection of Claims 38-53 under 35 U.S.C. 112, first paragraph, is withdrawn** in light of Applicant's amendments to the claims limiting the scope of the transgenic eukaryotic organisms to yeast.

Claim Rejections - 35 USC § 102

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the Applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the Applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the Applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. **The prior rejection of Claims 38 and 44 under 35 U.S.C. 102(b)** as being anticipated by Yan et al (Developmental Biology 140: 281-290, 1990; *of record in IDS) **is withdrawn** in light of Applicant's amendment to claim 38 to limit the scope of the vitellogenin cDNA to comprise SEQ ID NO:1, which is free of the prior art, and the amendment to claim 44 to limit the scope of the transgenic eukaryotic host to yeast. Yan et al do not teach SEQ ID NO:1 nor transgenic yeast.

7. **The prior rejection of Claims 38 and 44 under 35 U.S.C. 102(b)** as being anticipated by Grant et al (Mol. Biol. Cell 10: 4311-4326, 1999) **is withdrawn** in light of Applicant's amendment to claim 38 to limit the scope of the vitellogenin cDNA to comprise SEQ ID NO:1, which is free of the prior art, and the amendment to claim 44 to limit the scope of the transgenic eukaryotic host to yeast. Grant et al do not teach SEQ ID NO:1 nor transgenic yeast.

8. **The prior rejection of Claims 38-39 and 44-45 under 35 U.S.C. 102(b)** as being anticipated by Bradbury et al (J. Biol. Chem. 274(5):3159-3164, 1999) **is withdrawn** in light of Applicant's amendment to claim 38 to limit the scope of the vitellogenin cDNA to comprise SEQ ID NO:1, which is free of the prior art. Bradbury et al do not teach SEQ ID NO:1.

9. **The prior rejection of Claims 38-39 and 44-46 under 35 U.S.C. 102(b)** as being anticipated by Nusbaum et al (Nature Genetics 22: 388-393, 1999) **is withdrawn** in light of Applicant's amendment to limit the scope to a cDNA comprising SEQ ID NO:1. Nusbaum et al do not teach a cDNA comprising SEQ ID NO:1.

10. **The prior rejection of Claims 38-40 and 44 are rejected under 35 U.S.C. 102(a) and 102(e)** as being anticipated by Jacobs et al (U.S. 2001/0039335 A1) **is withdrawn** in light of Applicant's amendment to limit the scope to a cDNA comprising SEQ ID NO:1. Jacobs et al do not teach a cDNA comprising SEQ ID NO:1.

11. **Claims 45-46 stand and Claims 75-76 are newly rejected under 35 U.S.C. 102(a) and 102(e)** as being anticipated by Jacobs et al (U.S. 2001/0039335 A1).

This rejection is maintained for reasons of record in the office action mailed September 17, 2007 and re-stated below. The rejection has been re-worded slightly based upon Applicant's amendment filed February 15, 2008.

Jacobs et al disclose a polynucleotide encoding a polypeptide having similarity to a chicken vitellogenin (pg 127, [3373], col. 2, lines 17-20), wherein said polynucleotide may be expressed heterologously in yeast cells such as *Saccharomyces cerevisiae* or *Schizosaccharomyces pombe* (pg 165, [3844]), wherein the expression vector may be integrated into the host cell genome (pg 163, [3832]), wherein said polypeptide encoded by said polynucleotide may be expressed constitutively or tissue-specifically (pg 166, [3856]), wherein one of ordinary skill in the art would understand that constitutive or tissue-specific expression inherently requires the use of constitutive or tissue-specific promoter, respectively.

Jacobs et al disclose the polypeptide may be encoded by a cDNA [0028].

Applicant's Arguments

Applicant argues that because Jacobs et al disclose the expression of human sequences, Jacobs et al do not teach the elements of the instant claims, as argued above in response to the 112, 1st ¶ written description rejection, and incorporated herein.

Applicant's argument(s) has been fully considered, but is not persuasive. The examiner incorporates herein the response to Applicant's arguments regarding the 112, 1st ¶ written description rejection above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the Examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the Examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. **The prior rejection of Claims 38-41 and 44-53 under 35 U.S.C. 103(a)** as being unpatentable over Cregg et al (Molecular Biotechnology 16: 23-52, 2000) and Bradbury et al (J. Biol. Chem. 274(5):3159-3164, 1999) **is withdrawn** in light of Applicant's argument that the cited prior do not teach SEQ ID NO:1.

13. **Claims 38, 40-41, 43-53 and 75-78 are rejected under 35 U.S.C. 103(a)** as being unpatentable over Ding et al (AF017250, GI:4102880; January 5, 1999) in view of Cregg et al (Molecular Biotechnology 16: 23-52, 2000; *of record), Invitrogen™ Life Technologies, "Pichia expression vectors for constitutive expression and purification of recombinant proteins", Version F; September 3, 2002) and Ding et al (U.S. Patent 6,733,997).

This is a new rejection.

Determining the scope and contents of the prior art, and Ascertaining the differences between the prior art and the claims at issue

The claims are drawn to an expression vector comprising a vitellogenin cDNA comprising the sequence of SEQ ID NO:1 operably linked to a promoter, wherein the promoter is functional in a yeast host suitable for use as a feed or feed additive.

Ding et al taught a nucleic acid sequence possessing 100% identity to SEQ ID NO:1 (see attached Search Result of SEQ ID NO:1), said nucleic acid sequence encoding a vitellogenin precursor (Vtg1) mRNA.

Ding et al do not teach the nucleic acid sequence to be contained in an expression vector operably linked to a promoter, wherein the promoter is functional in a yeast host suitable for use as a feed or feed additive. However, at the time of the invention, Cregg et al teach that, at the time of publication, more than 200 different heterologous proteins expressed in the yeast *P. pastoris* had been published (pg 23, col. 2, Figure 1, Table 3), and a website has been created and maintained that lists such heterologous proteins. *P. pastoris* is a eukaryote capable of many of the post-translational modifications performed by higher eukaryotic cells, and is generally regarded as being faster, easier and less expensive to use than expression systems derived from higher eukaryotes, and usually gives higher expression levels (pg 24, col. 1). *P. pastoris* has long been used for the generation of yeast biomass or single-cell protein to be marketed primarily as high-protein animal feed (pg 24, col. 2, ¶1). Protease-deficient strains are available (pg 26, Table 1), as well as expression vectors for intracellular or secretion of the heterologous protein (pg 27,

Table 2), wherein said vectors comprise dominant drug-resistance markers that allow for enrichment of strains that receive multiple copies of foreign gene expression cassettes, wherein said vectors may integrate into the yeast host genome (pg 28, col. 1, ¶2; pg 29, col. 1). Cregg et al teach that the yeast GAP promoter is a strong constitutive promoter (pg 28, col. 2, ¶2). Cregg et al teach the use of pGAPZ and pGAPZα expression vectors (pg 27, Table 2).

Neither Ding et al nor Cregg et al teach the pGAPZA and pGAPZαC expression vectors. However, at the time of the invention, such expression vectors were commercially available (Invitrogen™).

Neither Ding et al nor Cregg et al teach that the expression vectors to encode a vitellogenin without a secretion signal (-SS), with the vitellogenin secretion signal (VtgSS) or with the alpha-factor secretion signal (αSS). However, Cregg et al teach that the heterologous polypeptide may be expressed intracellularly or secreted from the yeast, and the use of a secretion signal, e.g. the alpha factor secretion signal (αSS), for heterologous polypeptides should the artisan desired to heterologous polypeptide to be secreted into the medium (pg 25, col. 2, Secretion).

Neither Ding et al, Cregg et al nor teach (Invitrogen™) teach a vitellogenin secretory signal. However, at the time of the invention, Ding et al ('997) disclosed the use of a universal secrtetory signal derived from a piscine vitellogenin. It is well within the skills of the ordinary artisan to consider the presence or absence of a secretion signal, and to select a desired secretory signal as necessary.

Neither Ding et al nor Cregg et al teach that the amino acid contents, lipid contents and level of polyunsaturated fatty acids are increased in the transgenic yeasts expressing vitellogenin. However, absent evidence to the contrary, the recited increases in the recited subject matter is considered to be inherent features of the invention because the specification discloses that a host cell expressing vitellogenin inherently possesses increased levels of amino acids and lipids such as poly-unsaturated fatty acids as a consequence of expressing vitellogenin (pg 37, [00127]).

Resolving the level of ordinary skill in the pertinent art.

People of the ordinary skill in the art will be highly educated individuals such as doctors, scientists, or engineers, possessing advanced degrees, including M.D.'s and Ph.D.'s. Thus, these

people most likely will be knowledgeable and well-read in the relevant literature and have the practical experience in molecular biology, the creation of transgenic cells, and expressing heterologous proteins in a desired organism. Therefore, the level of ordinary skill in this art is high.

Considering objective evidence present in the application indicating obviousness or nonobviousness.

It would have been obvious to one of ordinary skill in the art to combine the vitellogenin cDNA of Ding et al with an expression vector as provided by Invitrogen™ for expression in a yeast such as *Pichia pastoris* with a reasonable chance of success because all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention. An artisan would be motivated to combine the vitellogenin cDNA of Ding et al with an expression vector as provided by Invitrogen™ for expression in a yeast such as *Pichia pastoris* because the art has long recognized said yeast as being an exceptional producer of heterologous proteins, and thus the artisan would be able obtain sufficient quantities of a vitellogenin for a desired purpose, e.g. crystallization or protein labeling studies.

Thus, the invention as a whole is *prima facie* obvious.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Kevin K. Hill, Ph.D. whose telephone number is 571-272-8036. The Examiner can normally be reached on Monday through Friday, between 9:00am-6:00pm EST.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Joseph T. Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kevin K. Hill, Ph.D./
Examiner, Art Unit 1633

/Q. JANICE LI/
Primary Examiner, Art Unit 1633